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Review article

The great debate: Surgical outcomes of laparoscopic versus laparotomic myomectomy. A meta-analysis to critically evaluate current evidence and look over the horizon

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### ABSTRACT

Myomectomy is one of the most common surgical procedure in the field of gynecology. However, the role of laparoscopic myomectomy is still debated for many factors, including surgical considerations, safety and fertility concerns, long-term outcomes, and cost-related issues. The aim of this study is to evaluate the surgical peri- and post-operative outcomes of laparoscopic and abdominal myomectomy. A systematic search for studies was performed up to June 2023 through MEDLINE, Pubmed, Embase. Studies reporting the comparison of surgical and obstetrical outcomes in laparoscopic versus laparotomic myomectomy were included for the following outcomes: time of surgery, estimated blood loss, decrease of postoperative hemoglobin, hospital stay, intraoperative complication rates, postoperative complications rates, postoperative analgesic use, postoperative pain at 24 h and pregnancy rate. The meta-analysis was performed using the Cochrane Review software. Fifty-six relevant articles were retrieved through the process of evidence acquisition. Eleven articles met inclusion criteria, for a total of 2,133 patients undergoing laparoscopic or laparotomic myomectomy. The estimated blood loss [standard mean differences (SMD) 0.72, IC 95 % 0.22 to 1.22], the hospital stays [SMD 3.12, IC 95 % 0.57 to 4.28], were significantly lower in laparoscopic than in open group. No statistically significant difference in intraoperative and post-operative complication rates, in pregnancy rate and others obstetrical outcomes between two surgical approaches were found. The findings of present metanalysis suggest that laparoscopic myomectomy offers multiple benefits, including reduced blood loss, shorter hospital stays, and less postoperative analgesic need, without a significant increase in complication rates and similar results in obstetrical outcomes when compared to abdominal myomectomy. However, the presence of few randomized studies on selected population may limit the generalizability of the findings to the entire population. Therefore, more well-designed studies or large population program data to draw definitive conclusions are therefore warranted.

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Abbreviations: UL, Uterine leiomyomas; FIGO, International Federation of Gynecology and Obstetrics; MeSH, Medical Subject Headings; BMI, Body mass index; SMD, Standardized mean difference; OR, Odds ratio; CI, Confidence interval; VAS, Visual analog scale.

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### Introduction

Uterine leiomyomas (UL) are the most common benign pelvic tumors in reproductive aged women [1–4]. UL can be classified according to International Federation of Gynecology and Obstetrics (FIGO) classification [5–7] as submucosal, intramural, subserosal, or transmural, depending on the location of occurrence: intracavitary, inside the myometrium or in the serosa of the uterus.

Clinically, UL can be asymptomatic or symptomatic. Symptomatic patients represent 25 % of women with UL and only these cases with symptoms or complications need a treatment [8]. Very common symptoms/signs referred by UL patients are heavy menstrual bleeding, lower abdominal pain and distention, micturition and defecation difficulties, and infertility. If medical treatment is ineffective, surgery may be necessary [9]. Hysterectomy may be considered as an option for patients who no longer have a desire for fertility. On the contrary, myomectomy is the typical operative management for patients who have a desire for fertility or refuse hysterectomy. Although symptomatic UL are widely treated by laparotomic myomectomy, laparoscopic myomectomy is a more attractive approach. The reasons for growing interest in laparoscopy rather than laparotomy are its pros, like minimal surgical access, fast recovery, less pain, and shorter hospital stay [10,11]. However, laparoscopic myomectomy has some cons, such as its need for longer operation times, together with more training for surgeons compared to laparotomic myomectomy [11,12]. Considering these points, the aim of this review and meta-analysis is to evaluate the surgical peri and postoperative outcomes and obstetrical outcomes of these two approaches in order to support surgeons in making a more aware choice, when treating UL.

### Materials and methods

### Search strategy

A search was performed up to June 2023 by two authors (I.C., T.G. A.) independently, within MEDLINE, Pubmed, Embase, selecting all relevant studies evaluating the comparison of surgical outcomes in women with UL after laparoscopic myomectomy and laparotomic myomectomy. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [13] and the Cochrane Handbook for Systematic Reviews of Interventions were followed during the development of this systematic review and *meta*-analysis.

The process of evidence acquisition combined the following keywords and their Medical Subject Headings (MeSH) terms: "Uterine Myomectomy" (MeSH Unique ID: D063186) combined with "Laparoscopy" (MeSH Unique ID: D010535) AND/OR "Laparotomy" (MeSH Unique ID: D007813).

Article abstracts, full text articles and cross-referenced studies identified from retrieved articles were screened independently by two review authors to identify studies that potentially meet the aims of this systematic review and *meta*-analysis. All duplicate records were removed.

### Selection of studies and methodologic quality assessment

The full texts of these potentially eligible articles were retrieved and independently assessed for eligibility by other two review team members. Any disagreement between them over the eligibility of particular articles was resolved through discussion with a third (external) collaborator. Two authors independently extracted data from articles about study characteristics and included populations, type of intervention and outcomes, using a pre-piloted standard form in order to ensure consistency. Any discrepancies were identified and resolved through discussion (with a third external collaborator where necessary). Key criteria for inclusion were: 1) original studies published in English, in peer-reviewed journals; 2) studies comparing laparoscopic and laparotomic approaches in patients undergoing myomectomy; 3) studies reporting on at least one of the outcomes measures of this *meta*-analysis.

The selected studies were comprehensively examined, and relevant data extracted for each paper. The selected information included: author, year of publication, main objective, study design (retrospective or prospective, mono or multicentric), mean age of patients, body mass index (BMI) of patients, number of UL removed, size of largest UL, localization of UL removed, estimated blood loss, operative time, hospital stay, intraoperative and post-operative complication rate, decrease of postoperative hemoglobin, pregnancy rate (the success rate for getting pregnant), uterine rupture, type of delivery, abortions.

The two authors (I.C., E.D.A.) carried out data extraction and quality assessment from all the retrieved studies based on full-text articles. Discrepancies between the investigators were resolved by consensus. The studies were then classified qualitatively according to the guidelines published in the Cochrane Handbook for Systematic Reviews of Interventions [14]. The risk of bias of non randomized studies included in the *meta*-analysis was assessed according to the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) [15]. The risk of bias of randomized studies included in the *meta*-analysis was assessed according to the Risk of Bias in randomized Trials [16]. The review had been prospectively registered in International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42023462941.

### Outcomes

The primary aim was to evaluate surgical outcomes in women with UL after laparoscopic myomectomy and laparotomic myomectomy, considering the following parameters: 1) time of surgery (minutes); 2) estimated blood loss (mL); 3) decrease of postoperative hemoglobin (g/dL); 4) hospital stay; 5) intra-operative complication rates; 6) postoperative complications rates; 7) postoperative analgesic use; 8) postoperative pain at 24 h; 9) pregnancy rate and other obstetrical outcomes.

### Statistical analysis

The data were analyzed using Cochrane Review software (Review Manager version 5.4 for Mac). Continuous outcomes were expressed as standardized mean difference (SMD). Dichotomous outcomes from each study were expressed as an odds ratio (OR) with a 95 % confidence interval (CI). Heterogeneity between studies was reported with the  $I^2$  statistic. A random-effects *meta*-analysis model was used if any heterogeneity was detected, whereas a fixed-effect model was used if no heterogeneity was identified. We decided to examine publication bias with Egger's test and funnel plots if the number of studies was 10 or above, since these analyses are underpowered otherwise.

### Results

### Study selection

The study selection is illustrated in Fig. 1.: the search resulted in 56 relevant articles. Eleven articles met inclusion criteria, for a total of 2133 patients [17–27]. The remaining studies were not included in the *meta*-analysis because they did not meet the inclusion criteria.

### Study characteristics and patient characteristics

The characteristics of included studies are detailed in Table 1 and Table 2. Among the 11 studies included: 1 study (9 %) was prospective observational [17], 3 (27.3 %) were retrospective observational [18–20]

and 7 (63.7 %) were randomized trials [21-27]. One study was published in 1995 [22], 1 study was published between 2000 and 2005 [26], 6 studies were published between 2006 and 2009 [17,21,23,24,25,27] and 3 studies were published after 2009 [18-20]. Of the total of 2133 patients, 1290 (60.5 %) underwent laparoscopic myomectomy, 843 (39.5 %) underwent laparotomic myomectomy. Of the 11 included studies, 4 studies reported the location of dominant UL removed [18,23,25,26]. Of 551 UL, 25 (4.6 %) were pedunculated, 192 (34.8 %) were subserous, 53 (9.6 %) were subserous-intramural, 276 (50.1 %) were intramural and 5 (0.9 %) were intramural-submucosal. 7 studies did not describe data about dominant UL type [17,19-22,24,27]. 10 studies reported the mean number of UL removed, for a total of 2081 patients [17-24,26,27]: in 3 studies the mean was less 2 ULs removed (789 patients, 38 %) [17-19], and in 7 studies it was greater than or equal to 2 ULs removed (1292 patients, 62 %) [20-24,26,27], with a maximum of 3.7 ULs. One study reported no data [25]. All studies reported the maximum diameter of the largest UL (cm), for a total of 2133 patients. Five studies [17,22–24,27] reported a dominant UL size less to 7 cm (443 patients, 20,7%), 6 studies [18–21,25,26] reported a dominant UL size greater than or equal to 7 cm (1,690 patients, 79.3 %). Laparoscopic and laparotomic surgical procedures were conducted by the same surgeons in 8 of the 11 studies included in the meta-analysis [17,19,22–27]. In the remaining three studies [18,20,21], it is not specified whether the same operators performed both surgical

### Table 1

The characteristics of included studies.

Study Characteristics	Studies (n = 11)	Patients (n = 2133)			
Pubblication Year					
Before 2000	1	40 (18.75 %)			
2000-2005	1	131 (6.14 %)			
2006–2009	6	495 (23.2 %)			
After 2009	3	1467 (68.8 %)			
Study Design					
Prospective	1	75 (3.52 %)			
Retrospective	3	1467 (68.8 %)			
Randomized	7	591 (27.7 %)			
Geographic location					
Europe	8	1074 (50.3 %)			
Asia	3	1059 (49.7)			

procedures. In addition, 8 of the 11 studies used a morcellation procedure to extract the myoma in the laparoscopic approach [17–20,22,24,26,27]. No laparoscopic procedures were robot-assisted.

The risk of bias assessment for the included studies is detailed in Tables S1 and S2.



Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

### Table 2

The characteristics of included studies.

Authors	Years	Туре	Pts	LA	AM	Inclusion criteria		
		of study				Number of myoma	Size of myoma (cm)	
Mais	1995	RCT	40	20	20	< 4	<6	
Seracchioli	2000	RCT	131	66	65	$\geq 1$	$\geq 5$	
Alessandri	2006	RCT	148	74	74	<4	<7	
Sesti	2006	RCT	100	50	50	<5	<10	
Holzer	2006	RCT	40	19	21	/	<10	
Cicinelli	2008	RCT	80	40	40	<3	<7	
Ji Tan	2008	RCT	52	26	26	<3	<10	
Kalogiannidis	2009	Obs	75	48	27	$\geq 1$	<9	
Kotani	2018	Retro	753	474	279	/	/	
Ordás	2022	Retro	254	112	142	$\geq 1$	$\geq 3$	
Catanese	2022	Retro	460	361	99	/	/	

RCT: Randomized Obs: Observational Retro: Retrospective.

### Outcomes

### Time of surgery

Ten studies with a total of 1,673 patients (926 in laparoscopic group and 744 in laparotomic group) were included in statistical analysis [17,18,20–27]. One study was excluded from the analysis because does not reported the mean of surgery time [19]. Time of surgery was analyzed in minutes. Non-significant differences were showed for the difference in mean time of surgery between group. A non-significant trend of increase in mean time of surgery was shown in in laparoscopic cohorts. The overall mean difference was -0.35 (95 % CI -0.72to 0.02, p =.06). Sensitivity analysis was performed according to the study design dividing Randomized (-0.39 (95 % CI -0.91 to 0.14, p =.15) and Non-Randomized (-0.28 (95 % CI -0.97 to 0.41, p =.43)) studies confirming the finding. (Fig. 2).

### Estimated blood loss

Seven studies with a total of 1,140 patients (677 in laparoscopic group and 463 in laparotomic group) were included in statistical analysis [17,20–25]. Four studies were excluded from the analysis because

did not report the mean of blood loss [18,19,26,27]. The estimated blood loss was analyzed in mL. The overall mean difference was 0.72 (95 % CI 0.22 to 1.22, p =.005) suggesting a reduced blood loss in laparoscopic cohorts. Sensitivity analysis was performed according to the study design dividing Randomized (0.69 (95 % CI -0.21 to 1.59, p =.14)) and Non-Randomized (0.82 (95 % CI 0.49 to 1.15, p <.001)) studies confirming the finding. (Fig. 3).

### Decrease of postoperative hemoglobin

Five studies with a total of 455 patients (238 in laparoscopic group and 217 in laparotomic group) were included in statistical analysis [17,23–25,27]. Six studies were excluded from the analysis because did not report the mean of decrease of postoperative hemoglobin [18–22,26]. Decrease of postoperative hemoglobin was analyzed in g/ dL.

The overall and sensitivity analysis did not reveal any statistically significant difference between the cohorts concerning the decrease of postoperative hemoglobin.

A non-significant trend in decrease of postoperative hemoglobin level was shown in laparoscopic cohorts. The overall mean difference was 1.07 (95 % CI -0.05 to 2.19, p =.06). Sensitivity analysis was performed according to the study design dividing Randomized (1.28 (95 % CI -0.08 to 2.63, p =.07)) and Non-Randomized (0.26 (95 % CI -0.22to 0.73, p =.29)) studies confirming the finding. (Fig. 4).

### Hospital stay

Eight studies with a total of 1,593 patients (890 in laparoscopic group and 703 in laparotomic group) were included in statistical analysis [17,18,20,23–27]. Three studies were excluded from the analysis because did not report the mean of hospital stay [19,21,22]. The overall mean difference was 3.12 (95 % CI 1.97 to 4.28p <.001) suggesting a reduced hospital stay in laparoscopic cohorts. Sensitivity analysis was performed according to the study design dividing Randomized (4.15 (95 % CI 2.37 to 5.93, p <.001)) and Non-Randomized (2.44 (95 % CI 0.57 to 4.30, p =.01)) studies confirming the finding. (Fig. 5).

### Intraoperative complications rate

Five studies with a total of 597 patients (294 in laparoscopic group

	Lapa	rotor	ny	Laparoscopy				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.3.1 RCT	1001 101-101-	100		1281623	1999 (Marine) 1997 (Marine)	1. 2 March 10		AND A REPORT OF ANY ADDRESS OF AN	<ul> <li>[10] K. S. M. S.</li></ul>
Alessandri 2006	85	14	74	98	13	74	10.6%	-0.96 [-1.30, -0.62]	
Cicinelli 2008	71	18	40	80	23	40	10.0%	-0.43 [-0.88, 0.01]	
Holzer 2006	68	22	21	99	37	19	8.5%	-1.01 [-1.67, -0.35]	
Ji Tan 2008	76	26	26	96	26	26	9.2%	-0.76 [-1.32, -0.19]	
Mais 1995	93	27	20	100	31	20	8.8%	-0.24 [-0.86, 0.39]	
Seracchioli 2000	89	27	65	100	38	66	10.6%	-0.33 [-0.68, 0.01]	
Sesti 2006	103	25	50	79	25	50	10.2%	0.95 [0.54, 1.37]	
Subtotal (95% CI)			296			295	67.8%	-0.39 [-0.91, 0.14]	
Heterogeneity: Tau <sup>2</sup> =	0.44; Ch	i² = 5	6.23, di	f= 6 (P <	0.00	001); l²	= 89%		
Test for overall effect:	Z=1.44	(P = 0	0.15)						
1.3.2 No RCT									
Kalogiannidis 2009	83	24	27	68	21	48	9.7%	0.67 [0.19, 1.16]	
Kotani 2018	127	48	279	148	58	474	11.5%	-0.38 [-0.53, -0.24]	
Ordas 2022	95	37	142	147	64	112	11.0%	-1.02 [-1.29, -0.76]	
Subtotal (95% CI)			448			634	32.2%	-0.28 [-0.97, 0.41]	
Heterogeneity: Tau <sup>2</sup> =	0.34; Ch	i² = 3	9.47, di	= 2 (P <	0.00	001); I <sup>2</sup>	= 95%		
Test for overall effect:	Z = 0.80	(P = 0	0.43)						
Total (95% CI)			744			929	100.0%	-0.35 [-0.72, 0.02]	-
Heterogeneity: Tau <sup>2</sup> =	0.31; Ch	i² = 9	6.53, di	f=9(P<	0.00	001); l <sup>=</sup>	= 91%		
Test for overall effect:	Z=1.86	(P = (	0.06)						-2 -1 U 1 2
Test for subaroup diffe	erences:	Chi <sup>2</sup>	= 0.06.	df = 1 (P)	= 0.8	1), I <sup>2</sup> =	0%		Laparotomy Laparoscopy

Fig. 2. Forest plot of comparison on time of surgery between laparotomic myomectomy and laparoscopic myomectomy.

	Lapa	Laparotomy Laparoscopy				ру		Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
1.1.1 RCT											
Cicinelli 2008	186	44	40	133	29	40	14.4%	1.41 [0.92, 1.90]			
Holzer 2006	115	64	21	71	80	19	13.1%	0.60 [-0.04, 1.23]	+ <b>-</b>		
Ji Tan 2008	72	19	26	96	32	26	13.7%	-0.90 [-1.47, -0.33]			
Mais 1995	230	44	20	200	50	20	13.1%	0.62 [-0.01, 1.26]			
Sesti 2006	188.6	1.3	50	154.2	29	50	14.7%	1.66 [1.21, 2.12]			
Subtotal (95% CI)			157			155	69.0%	0.69 [-0.21, 1.59]			
Heterogeneity: Tau <sup>2</sup> = 0.98; Chi <sup>2</sup> = 53.99, df = 4 (P < 0.00001); l <sup>2</sup> = 93%											
Test for overall effect:	Z=1.49	(P = 0	).14)								
1.1.2 No RCT											
Kalogiannidis 2009	351	219	27	246	161	48	14.5%	0.57 [0.08, 1.05]			
Kotani 2018	554	536	279	207	225	474	16.5%	0.93 [0.78, 1.09]			
Subtotal (95% CI)			306			522	31.0%	0.82 [0.49, 1.15]			
Heterogeneity: Tau <sup>2</sup> =	: 0.03; Cł	ni² = 2.	.03, df=	= 1 (P =	0.15);	l² = 519	%				
Test for overall effect:	Z = 4.89	(P < 0	0.00001	)							
Total (95% CI)			463			677	100.0%	0.72 [0.22, 1.22]			
Heterogeneity: Tau <sup>2</sup> =	: 0.38; Cł	ni² = 5	6.22, di	f=6 (P <	< 0.00	001); I²	= 89%				
Test for overall effect:	Z=2.84	(P = 0	0.005)						-2 -1 U I Z		
Test for subaroup diff	ferences:	Chi <sup>2</sup> :	Laparotoniy Laparoscopy								

Fig. 3. Forest plot of comparison on estimated blood loss between laparotomic myomectomy and laparoscopic myomectomy.

	Lapa	roton	tomy Laparoscopy			ру		Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl		
1.4.1 RCT											
Alessandri 2006	2.2	0.5	74	1.1	0.5	74	20.3%	2.19 [1.78, 2.60]			
Cicinelli 2008	2.5	0.3	40	1.5	0.4	40	19.6%	2.80 [2.18, 3.43]			
Ji Tan 2008	1.2	0.6	26	1.6	0.6	26	19.8%	-0.66 [-1.22, -0.10]			
Sesti 2006	0.7	0.3	50	0.5	0.2	50	20.3%	0.78 [0.37, 1.19]			
Subtotal (95% CI)			190			190	79.9%	1.28 [-0.08, 2.63]			
Heterogeneity: Tau <sup>2</sup> = 1.85; Chi <sup>2</sup> = 93.59, df = 3 (P < 0.00001); l <sup>2</sup> = 97%											
Test for overall effect:	Z = 1.84	(P = 0	).07)								
1.4.2 No RCT											
Kalogiannidis 2009	1.7	1	27	1.5	0.6	48	20.1%	0.26 [-0.22, 0.73]			
Subtotal (95% CI)			27			48	20.1%	0.26 [-0.22, 0.73]	-		
Heterogeneity: Not ap	plicable										
Test for overall effect:	Z = 1.07	(P = 0	).29)								
Total (95% CI)			217			238	100.0%	1.07 [-0.05, 2.19]			
Heterogeneity: Tau <sup>2</sup> =	1.56; Ch	i <sup>2</sup> = 1	08.05,	df = 4 (P	< 0.0	0001);1	²= 96%				
Test for overall effect:	Z=1.88	(P = 0	0.06)						Laparotomy Laparoscopy		
Test for subgroup differences: Chi <sup>2</sup> = 1.93, df = 1 (P = 0.16), l <sup>2</sup> = 48.1%											

Fig. 4. Forest plot of difference in decrease of postoperative hemoglobin level after laparotomic myomectomy and laparoscopic myomectomy.

and 303 in laparotomic group) were included in statistical analysis [17,18,22,24,27]. Six studies were excluded from the analysis because did not report the occurence of intraoperative complications rate [19–21,22,25,27].

Only one study [18] analyzed intraoperative complications using the Clavien-Dindo classification, not dividing them into grade of severity. In view of the lack of classification in the other studies, the occurrence of complications was considered. The main intraoperative complications were injuries to internal organs such as bowel, uterus, bladder, and vascular injuries.

The analysis did not reveal any statistically significant difference between cohorts in occurrence of intraoperative complications. The OR was 0.89 (95 % CI 0.36 to 2.17p =.80). Sensitivity analysis was performed according to the study design dividing Randomized (0.25 (95 % CI 0.03 to 2.28, p =.22)) and Non-Randomized (1.14 (95 % CI 0.43 to 3.02, p =.79)) studies confirming the finding. (Fig. 6). Postoperative complications rate

Three studies with a total of 754 patients (493 in laparoscopic group and 261 in laparotomic group) were included in statistical analysis [18,19,22]. 8 studies were excluded from the analysis because did not report the mean of postoperative complications rate [17,20,21,23–27]. One study [18] analyzed postoperative complications using the Clavein-Dindo classification, dividing them into grade of severity. In only one study were postoperative complications recorded in terms of early complications (<30 days, > G2) and long-term complications (>30 days, > G2) [19].

In view of the lack of classification in the other studies, the occurrence of complications was considered. The analysis did not reveal any statistically significant difference between the cohorts concerning postoperative complications rate. The OR was 1.35 (95 % CI 0.72 to 2.52p = .35). Sensitivity analysis was performed according to the study design dividing Randomized (1.00 (95 % CI 0.06 to 17.18, p =.99)) and Non-Randomized (1.37 (95 % CI 0.72 to 2.60, p =.34)) studies confirming the finding. (Fig. 7).

	Lapa	aroton	ny	Lapa	rosco	ру		Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
1.2.1 RCT											
Alessandri 2006	2	0.5	74	1.5	0.5	74	13.9%	0.99 [0.65, 1.34]			
Cicinelli 2008	3.3	0.5	40	2.1	0.6	40	13.6%	2.15 [1.60, 2.71]			
Ji Tan 2008	2.04	0.66	26	1.81	0.57	26	13.6%	0.37 [-0.18, 0.92]		+	
Seracchioli 2000	5.9	1.4	65	3.16	1.5	66	13.8%	1.88 [1.46, 2.29]			
Sesti 2006	4.1	0.05	50	2.2	0.06	50	4.0%	34.14 [29.30, 38.98]			•
Subtotal (95% CI)			255			256	58.9%	4.15 [2.37, 5.93]			
Heterogeneity: Tau <sup>2</sup> = 3.55; Chi <sup>2</sup> = 206.67, df = 4 (P < 0.00001); l <sup>2</sup> = 98%											
Test for overall effect:	Z= 4.57	(P < 0	.00001	)							
1.2.2 No RCT											
Kalogiannidis 2009	4.2	0.8	27	1.8	0.5	48	13.2%	3.81 [3.02, 4.59]			$\rightarrow$
Kotani 2018	11.7	3.9	279	3.5	1.8	474	14.0%	2.96 [2.75, 3.17]		-	
Ordas 2022	5	1.13	142	4	2.1	112	13.9%	0.61 [0.36, 0.87]			
Subtotal (95% CI)			448			634	41.1%	2.44 [0.57, 4.30]			
Heterogeneity: Tau <sup>2</sup> =	2.66; Cł	ni² = 21	4.43, 0	if = 2 (P	< 0.00	0001); P	²= 99%				
Test for overall effect:	Z = 2.56	(P = 0	.01)								
Total (05% CI)			703			000	100.0%	3 4 2 14 07 4 201			
Total (95% CI)			705			890	100.0%	3.12 [1.97, 4.28]			-
Heterogeneity: Tau <sup>2</sup> =	2.47; Cl	$ni^2 = 44$	46.01, 0	if = 7 (P	< 0.00	)001); F	*= 98%		-4 -2	2 0 2	4
Test for overall effect:	Z = 5.30	(P < 0	.00001	)					La	parotomy Laparoscopy	
Test for subgroup differences: Chi <sup>2</sup> = 1.69, df = 1 (P = 0.19), $l^2$ = 40.9%											

Fig. 5. Forest plot of comparison on length of stay in hospital between laparotomic myomectomy and laparoscopic myomectomy.

	Laparot	omy	Laparos	сору		Odds Ratio	Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl				
1.5.1 RCT											
Alessandri 2006	0	74	2	74	8.6%	0.19 (0.01, 4.12)					
Cicinelli 2008	0	40	1	40	7.6%	0.33 [0.01, 8.22]					
Mais 1995	0	20	0	20		Not estimable					
Subtotal (95% CI)		134		134	16.2%	0.25 [0.03, 2.28]					
Total events	0		3								
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 0.05,	df = 1 (P =	= 0.82);	l² = 0%						
Test for overall effect:	Z = 1.23 (F	° = 0.22	)								
1.5.2 No RCT											
Kalogiannidis 2009	1	27	2	48	13.3%	0.88 [0.08, 10.23]					
Ordas 2022	9	142	6	112	70.5%	1.20 [0.41, 3.46]					
Subtotal (95% CI)		169		160	83.8%	1.14 [0.43, 3.02]	-				
Total events	10		8								
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 0.05,	df = 1 (P =	= 0.82);	l² = 0%						
Test for overall effect:	Z = 0.26 (F	° = 0.79	)								
Total (95% CI)		303		294	100.0%	0.89 [0.36, 2.17]	-				
Total events	10		11								
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 1.64	df = 3 (P =	= 0.65);	l² = 0%						
Test for overall effect:	Z = 0.26 (F	° = 0.80	)				Laparotomy Laparoscopy				
Test for subgroup diffe	Test for subgroup differences; Chi <sup>2</sup> = 1.52, df = 1 (P = 0.22), l <sup>2</sup> = 34.2%										

Fig. 6. Forest plot of comparison on intraoperative complications incidence between laparotomic myomectomy and laparoscopic myomectomy.

### Postoperative analgesic use

Two studies with a total of 198 patients (98 in laparoscopic group and 100 in laparotomic group) were included in statistical analysis [25,27]. Nine studies were excluded from the analysis because did not report the mean of postoperative analgesic use [17–24,27]. However, one [25] of the two studies reported that all patients in both laparoscopic and laparotomic cohorts assumed analgesics after surgery, making the *meta*-analysis impractical. The other study available reported a statistically significant reduction in the use of analgesics in patients undergoing laparoscopic myomectomy. [27]. and 171 in laparotomic group) were included in statistical analysis [21,23,25,27]. 7 studies were excluded from the analysis because did not report the mean of postoperative analgesic use [17–20,22,24,27]. Postoperative pain was evaluated with a visual analog scale (VAS). The analysis did not reveal any statistically significant difference between the cohorts concerning postoperative pain at 24 h. The OR was 0.09 (95 % CI –0.23 to 0.41p = .58). (Fig. 8).

### Pregnancy rate and obstetrical outcomes

Eight studies were excluded from the analysis because did not report the pregnancy rate [17,19,21–25,27]. Three studies with a total of 1,063 patients (642 in laparoscopic group and 480 in laparotomic group) were included in statistical analysis [18,20,26]. The analysis did not reveal

## Postoperative pain at 24 h

Four studies with a total of 340 patients (169 in laparoscopic group

	Laparot	omy	Laparos	сору		Odds Ratio		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl		
1.6.1 RCT										
Mais 1995	1	20	1	20	4.9%	1.00 [0.06, 17.18]				
Subtotal (95% CI)		20		20	4.9%	1.00 [0.06, 17.18]				
Total events	1		1							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 0.00 (I	P = 1.00	))							
1.6.2 No RCT										
Catanese 2022	0	99	3	361	4.4%	0.51 [0.03, 10.05]		· · · ·		
Ordas 2022	29	142	17	112	90.7%	1.43 [0.74, 2.77]				
Subtotal (95% CI)		241		473	95.1%	1.37 [0.72, 2.60]				
Total events	29		20							
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi	<sup>2</sup> = 0.44	, df = 1 (P :	= 0.51);	I <sup>2</sup> = 0%					
Test for overall effect:	Z = 0.95 (I	P = 0.34	4)							
Total (95% CI)		261		493	100.0%	1.35 [0.72, 2.52]				
Total events	30		21							
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>a</sup>	<sup>2</sup> = 0.48	, df = 2 (P :	= 0.79);	I <sup>2</sup> = 0%		102		-	
Test for overall effect:	Z = 0.93 (I	P = 0.36	5)				0.02	Lanarotomy Lanaroscony	50	
Test for subgroup differences: Chi <sup>2</sup> = 0.04, df = 1 (P = 0.83), l <sup>2</sup> = 0%										

Fig. 7. Forest plot of comparison on postoperative complications incidence between laparotomic myomectomy and laparoscopic myomectomy.

	Lapa	rotor	ny	Lapa	rosco	ру		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Alessandri 2006	2.8	1.8	74	3.1	1.5	74	33.7%	-0.18 [-0.50, 0.14]	
Holzer 2006	4.4	1.6	21	3.5	1.8	19	17.0%	0.52 [-0.11, 1.15]	
Ji Tan 2008	4.15	0.9	26	4.26	1.08	26	20.5%	-0.11 [-0.65, 0.44]	
Sesti 2006	4.2	2.4	50	3.45	2.6	50	28.8%	0.30 [-0.10, 0.69]	+ <b>-</b>
Total (95% CI)			171						
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:	: 0.05; Cl Z = 0.56	ni² = 5 (P = 1	-2 -1 0 1 2 Laparotomy Laparoscopy						

Fig. 8. Forest plot of comparison on postoperative pain incidence in 24 h after laparotomic myomectomy and laparoscopic myomectomy.

any statistically significant difference between the cohorts concerning pregnancy rate. The OR was 0.78 (95 % CI 0.42 to 1.45p = .43) (Fig. 9). Details about other obstetric outcomes, including uterine rupture, type of delivery, and the number of abortions were reported in two studies with a total of 388 patients [18,26]. In the laparotomic group, there were 37 cesarean deliveries and 11 vaginal deliveries, whereas in the laparoscopic group, there were 29 cesarean deliveries and 22 vaginal deliveries. However, statistical analysis did not reveal any significant differences between the two groups (OR: 1.16 [95 % CI 0.49 to 2.73p =.73] and OR: 0.42 [0.13 to 1.38p =.15], respectively) (Figs. S1 and S2). The rate of abortions was similar groups (OR: 0.51, 95 % CI 0.18 to 1.46, p =.21). No cases of uterine ruptures were reported either in two groups group [18,26] (Fig. S3).

### Discussion

The present *meta*-analysis summarizes the highest-quality evidence available in the literature on the comparison of surgical outcomes in women with UL after laparoscopic myomectomy and laparotomic myomectomy. The pooled data analysis indicates that laparoscopic myomectomy offers several advantages, including shorter hospital stays, reduced blood loss and postoperative analgesic use compared with laparotomic approach. Nevertheless, there was no statistical difference in rate of intra-operative or post-operative complications between laparoscopic and laparotomic approach. Furthermore, no statistically significant difference emerged in the pregnancy rate and in other obstetrical outcomes.

Myomectomy is a widely performed surgical procedure employed for



Fig. 9. Forest plot of comparison on pregnancy rate after laparotomic myomectomy and laparoscopic myomectomy.

the management of symptomatic UL. Over in the past few decades, laparoscopic surgery emerged as a prominent alternative to conventional laparotomic approach for myomectomy.

Laparoscopic surgery, involving the use of small abdominal incisions and fiber-optic instruments, facilitates the surgeon's ability to conduct the operation with greater visualization, precision, and good aesthetic outcome of the resulting scars [28].

Some authors have examined the evidence regarding the surgical outcomes of the two approaches, but the results have been conflicting. A prospective study analyzed 213 patients undergoing myomectomy and found no significant differences in surgical and clinical outcomes between laparoscopic and laparotomic surgery. [29]. Some authors reported a significantly reduced hemoglobin drop and blood loss, a shorter hospitalization, regarding operative complications rate [17,24,27,30]. Nevertheless, the laparoscopic approach for myomectomy is still a debated procedure for the potential limitation. Critical factors to consider are the surgeon's experience, the suitability of the patient, and the size, location, and number of uterine fibroids. Laparoscopic myomectomy, often require specialized surgical skills and training. Surgeons need to be proficient in using laparoscopic instruments and techniques. Inexperienced surgeons may face challenges when performing complex laparoscopic procedures, potentially leading to longer surgery times or increased risk of complications. Moreover, laparoscopy can be limited when dealing with large, multiple, or deeply located UL. The size and location can make it challenging to perform laparoscopic procedures. In such cases, abdominal surgery may be preferred because it provides the surgeon with more direct access and visibility.

One author, analyzed 444 patients, demonstrated that the size and type of UL serve as the most reliable indicators of surgical complexity and the potential for complications during and after surgery. Notably, when a patient presents with a minimum of two intramural or subserosal UL, with at least one exceeding 8 cm in size, it may be advisable to consider a laparotomic approach as the preferred surgical method [18]. Furthermore, it is important to consider that studies designed for laparoscopic myomectomy often have stringent inclusion criteria, thereby limiting the assessment of more challenging cases. Most studies focus on patients with fibroids smaller than 10 cm or with three to four fibroids. In any case, the most widely recognized contraindications to diagnostic laparoscopy are: Multiple fibroids, more than three fibroids measuring > 7 cm, uterine volume > 20 gestational weeks, single fibroid > 15 cm, women who have completed their reproductive cycle and desire hysterectomy, any medical condition contraindicating prolonged anesthesia for laparoscopic surgery [31].

A growing body of evidence suggests that minimally invasive surgical procedures tend to incur higher costs compared to abdominal surgery [32]. However, it's important to consider the advantages offered to patients, shorter recovery periods, and a quicker return to work [32,18]. These factors may exert a notable influence on the overall societal costs associated with treatment. [32,21].

The selection between these two surgical approaches should be decided upon a comprehensive evaluation of the patient's clinical profile, UL characteristics (number, size and location), surgeon proficiency, and available resources. The principal objective is the attainment of an optimal therapeutic outcome, with a judicious balance between risk reduction and patient benefit.

Another point deserving attention is the role of intra-abdominal morcellation in undiagnosed uterine sarcoma [33,34]. Although rare, we have to take into account that morcellation of undiagnosed uterine sarcoma might be related to worse oncologic outcomes for those patients (upstaged from stage I to stage IV due to dissemination of uterine malignancies). In the current scenario, in-bag morcellation should be used during minimally invasive myomectomy [34,35], however, a comprehensive counseling of the patient, stating that there is currently no Level I evidence that endobag morcellation can reduce the risk of spillage of any potential occult sarcoma, must be clearly conducted.

In addition, the uterine cavity exploration by hysteroscopy could be

useful in preoperative time [36,37]. The study of endometrial cavity and the possibility to perform targeted biopsies, could help in choosing the most correct surgical approach [38].

The strengths of this *meta*-analysis are as follows: first, this work represents the most up-to-date *meta*-analysis aiming to establish the advantages and disadvantages of laparoscopic and laparotomic myomectomy, in order to tailor surgical therapy by selecting patients appropriately. Second, more than half of studies *meta*-analyzed, seven were randomized trials. Third, the sub-analysis includes the main surgical outcomes to be considered for a comprehensive evaluation of the two surgical approaches analyzed, by assessing individual values of mean differences and odds ratio according on the various outcomes. In addition, the main studies present in the literature were included, respecting the inclusion criteria to obtain uniform results from the statistical analysis.

The present *meta*-analysis has some limitations. First, in some included studies, the surgeon have chosen the myomectomy approach according to indications, surgical experience and patient characteristics such as the number, size and location of UL. The surgeon's experience affects all the outcomes analyzed, although the skills of the operators is not known (or at least clearly defined) for all studies. Second, patients' characteristics such as size, number, and location of UL were not reported in all studies. Third, those studies did not take into account the need to perform in-bag morcellation. This feature might influence the operative variables (in particular operative time) of the current adopted laparoscopic approach.

### Conclusion

Laparoscopic myomectomy, compared with laparotomic myomectomy, was associated with significantly shorter hospitalization days, postoperative analgesic use and estimated blood loss. The laparoscopic approach could be a valid alternative to laparotomic one, in selected patients. Therefore, more well-designed studies or large population program data to draw definitive conclusions are therefore warranted.

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### CRediT authorship contribution statement

Andrea Giannini: Visualization, Resources, Project administration, Methodology, Formal analysis, Conceptualization. Ilaria Cuccu: Writing – original draft, Software, Investigation, Formal analysis, Data curation. Tullio Golia D'Auge: Writing – original draft, Investigation, Data curation. Emanuele De Angelis: Writing – original draft, Investigation, Data curation. Antonio Simone Laganà: Supervision, Methodology. Vito Chiantera: Supervision. Donatella Caserta: Supervision. Salvatore Giovanni Vitale: Visualization, Validation. Ludovico Muzii: Validation, Conceptualization. Ottavia D'Oria: Formal analysis. Giorgia Perniola: Supervision, Software. Giorgio Bogani: Validation, Project administration, Conceptualization. Violante Di Donato: Visualization, Supervision, Project administration, Conceptualization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability statement

All data relevant to the study are included in the article or uploaded as supplementary information

### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2024.03.045.

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